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EXAMINER	
TRAN, MY CHAU T	

ART UNIT	PAPER NUMBER
1639	

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25

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/748,793	Applicant(s) AEBERSOLD ET AL.	
	Examiner My-Chau T. Tran	Art Unit 1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23 and 44-52* is/are pending in the application.

4a) Of the above claim(s) *24-43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-23 and 44-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *24*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 9/10/2003 has been entered.

Status of Claims

2. Applicant's amendment filed 8/7/2003 in Paper No. 20 is acknowledged and entered. Claims 1, and 13 are amended by the amendment. Claims 51-52 are added by the amendment.

3. Claims 1-52 are pending.

Election/Restrictions

4. Claims 24-43 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 10 (7/26/02).

Withdrawn Rejections

5. The previous rejections under 35 USC 112, second paragraph, for claims 13-23 have been withdrawn in view of applicant's amendments of claim 13 (e.g. the addition of the

limitation of "by comparison to a standard corresponding to said polypeptide, or said peptide fragment thereof".

6. The previous rejection under 35 USC 102(b) as being anticipated by Yates, III (*J. Mass Spectrom.*; 33(1):1-19; 1998) or Link et al. (*Nat. Biotechnol.*; 17(7):676-682; 1999) for claims 1-2 and 8-12 has been withdrawn in view of applicant's amendments of claim 1, and arguments have been considered but are moot in view of the new ground(s) of rejection.

7. The previous rejection under 35 USC 102(b) as being anticipated by Yates, III (*J. Mass Spectrom.*; 33(1):1-19; 1998) or Link et al. (*Nat. Biotechnol.*; 17(7):676-682; 1999) for claims 1-2, 8-12, 44, 45, and 47-50 has been withdrawn in view of applicant's amendments of claim 1, and arguments have been considered but are moot in view of the new ground(s) of rejection.

8. The previous rejection under 35 USC 103(a) as being obvious over Yates, III (*J. Mass Spectrom.*; 33(1):1-19; 1998) or Link et al. (*Nat. Biotechnol.*; 17(7):676-682; 1999) in view of Mann (*Nat. Biotechnol.*; 17(10):954-955; 1999) or Gygi et al. (*Nat. Biotechnol.*; 17(10):994-999; 1999) for claims 1, 3, 13-14, and 20-23 has been withdrawn in view of applicant's amendments of claims 1 and 13, and arguments have been considered but are moot in view of the new ground(s) of rejection.

9. The previous rejection under 35 USC 103(a) as being obvious over Yates, III (*J. Mass Spectrom.*; 33(1):1-19; 1998) or Link et al. (*Nat. Biotechnol.*; 17(7):676-682; 1999) in view of Masselon et al. (*Anal. Chem.*; 72:1918-1924; 2000) for claims 1, 4-8 and 15-19 has been withdrawn in view of applicant's amendments of claim 1, and arguments have been considered but are moot in view of the new ground(s) of rejection.

10. The previous rejection under 35 USC 103(a) as being obvious over Yates, III (*J. Mass Spectrom.*; 33(1):1-19; 1998) or Link et al. (*Nat. Biotechnol.*; 17(7):676-682; 1999) for claims 1, 44, and 46 has been withdrawn in view of applicant's amendments of claim 1, and arguments have been considered but are moot in view of the new ground(s) of rejection.

11. Claims 1-23, and 44-52 are treated on the merit in this Office Action.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 1-12, and 44-50 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (This is a written description rejection)

The instant claim 1 briefly recites a method of identifying a polypeptide. The method steps comprise of a) determining at least two characteristics of the polypeptide wherein one of the characteristic (first characteristic) is the mass of the peptide determined by mass spectrometry; b) comparing these characteristic to an annotated polypeptide index, wherein the annotated polypeptide index is not a sequence database; and c) identifying one or more polypeptides in the annotated polypeptide index having these characteristics.

The specification disclosure does not sufficiently teach the method of identifying a polypeptide wherein the method step of generating(creating) a reference polypeptide database (an annotated polypeptide index) for a specific "class" species is excluded.

The specification description is directed to the method of identifying a polypeptide wherein the first step is to generate/create a reference database (an annotated polypeptide index) that is representative of any number of polypeptides in a sample and using this database to identify the polypeptide of any sample (pg. 7, lines 1-12; pg. 12, lines 1-8; pg. 18, lines 15-29; pg. 26, lines 12-30) and then using this reference database to identify the polypeptide in the sample (pg. 7, lines 1-12; pg. 27, lines 12-30). This method clearly does not provide an adequate representation regarding the claimed method of identifying a polypeptide wherein the method step of generating(creating) a reference polypeptide database (an annotated polypeptide index) for a specific "class" species is excluded. The specification examples are drawn to the method of identifying a polypeptide wherein the first step of the method is to generate/create a reference polypeptide database for a specific "class" species and then using this database to identifying a polypeptide in a sample (Example I and II of pg. 66-78). The specification does not teach the method of identifying a polypeptide wherein the method step of generating(creating) a reference polypeptide database (an annotated polypeptide index) for a specific "class" species is excluded.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons

of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

With the exception of the method of identifying a polypeptide wherein the method step of generating(creating) a reference polypeptide database (an annotated polypeptide index) for a specific "class" species and then using this database to identifying a polypeptide in the sample disclosed by the specification, the skilled artisan cannot envision the method of identifying a polypeptide wherein the method step of generating(creating) a reference polypeptide database (an annotated polypeptide index) for a specific "class" species is excluded. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying a polypeptide by using a reference database. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

In the present instance, the claimed method of identifying a polypeptide comprises the step of a) determining at least two characteristics of the polypeptide wherein one of the characteristic (first characteristic) is the mass of the peptide determined by mass spectrometry; b) comparing these characteristic to an annotated polypeptide index, wherein the annotated polypeptide index is not a sequence database; and c) identifying one or more polypeptides in the annotated polypeptide index having these characteristics. The specification does not teach the method of identifying a polypeptide wherein the method step of generating(creating) a reference polypeptide database (an annotated polypeptide index) for a specific "class" species is excluded. Therefore, only the method of identifying a polypeptide wherein the method step of generating(creating) a reference polypeptide database (an annotated polypeptide index) for a specific "class" species and then using this database to identifying a polypeptide in a sample, but not the full breadth of the claim method meet the written description provision of 35 U.S.C 112, first paragraph.

14. Claims 13-23, and 51-52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (This is a written description rejection)

The instant claim 13 briefly recites a method of identifying a polypeptide. The method steps comprise of a) determining at least two characteristics of the polypeptide wherein one of the characteristic (first characteristic) is the mass of the peptide determined by mass spectrometry; b) comparing these characteristic to an annotated polypeptide index, wherein the

annotated polypeptide index is not a sequence database; c) identifying one or more polypeptides in the annotated polypeptide index having these characteristics; and d) quantitating the amount of identified polypeptide.

The specification disclosure does not sufficiently teach the method of identifying a polypeptide wherein the method step of generating(creating) a reference polypeptide database (an annotated polypeptide index) for a specific "class" species is excluded.

The specification description is directed to the method of identifying a polypeptide wherein the first step is to generate/create a reference database (an annotated polypeptide index) that is representative of any number of polypeptides in a sample and using this database to identify the polypeptide of any sample (pg. 7, lines 1-12; pg. 12, lines 1-8; pg. 18, lines 15-29; pg. 26, lines 12-30) and then using this reference database to identify the polypeptide in the sample (pg. 7, lines 1-12; pg. 27, lines 12-30). This method clearly does not provide an adequate representation regarding the claimed method of identifying a polypeptide wherein the method step of generating(creating) a reference polypeptide database (an annotated polypeptide index) for a specific "class" species is excluded. The specification examples are drawn to the method of identifying a polypeptide wherein the first step of the method is to generate/create a reference polypeptide database for a specific "class" species and then using this database to identifying a polypeptide in a sample (Example I and II of pg. 66-78). The specification does not teach the method of identifying a polypeptide wherein the method step of generating(creating) a reference polypeptide database (an annotated polypeptide index) for a specific "class" species is excluded.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was

in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

With the exception of the method of identifying a polypeptide wherein the method step of generating(creating) a reference polypeptide database (an annotated polypeptide index) for a specific "class" species and then using this database to identifying a polypeptide in the sample disclosed by the specification, the skilled artisan cannot envision the method of identifying a polypeptide wherein the method step of generating(creating) a reference polypeptide database (an annotated polypeptide index) for a specific "class" species is excluded. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying a polypeptide by using a reference database. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it

obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

In the present instance, the claimed method of identifying a polypeptide comprises the step of a) determining at least two characteristics of the polypeptide wherein one of the characteristic (first characteristic) is the mass of the peptide determined by mass spectrometry; b) comparing these characteristic to an annotated polypeptide index, wherein the annotated polypeptide index is not a sequence database; c) identifying one or more polypeptides in the annotated polypeptide index having these characteristics; and d) quantitating the amount of identified polypeptide. The specification does not teach the method of identifying a polypeptide wherein the method step of generating(creating) a reference polypeptide database (an annotated polypeptide index) for a specific "class" species is excluded. Therefore, only the method of identifying a polypeptide wherein the method step of generating(creating) a reference polypeptide database (an annotated polypeptide index) for a specific "class" species and then using this database to identifying a polypeptide in a sample, but not the full breadth of the claim method meet the written description provision of 35 U.S.C 112, first paragraph.

15. Claims 1-23, and 44-52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (This is a scope written description rejection)

The instant claimed methods briefly recite the method of identifying a polypeptide wherein the determined characteristic of the polypeptide in the sample is compared to the

characteristic found in an annotated polypeptide index with the proviso that the annotated polypeptide index is not a sequence database to identify the polypeptide in the sample.

The specification disclosure does not sufficiently teach the method of identifying a polypeptide using ***any*** reference polypeptide database that is not a sequence database (e.g. both commercial and known peptide databases such as MASCOT and MOWSE, which are peptide databases for molecular weights of peptides) for identification of the polypeptide in the sample.

The specification description is directed to the method of identifying a polypeptide wherein the first step is to generate/create a reference database (an annotated polypeptide index) that is representative of any number of polypeptides in a sample and using this database to identify the polypeptide of any sample (pg. 7, lines 1-12; pg. 12, lines 1-8; pg. 18, lines 15-29; pg. 26, lines 12-30) and then using this reference database to identify the polypeptide in the sample (pg. 7, lines 1-12; pg. 27, lines 12-30). This method clearly does not provide an adequate representation regarding scope of the type of database to be use for the identification of the polypeptide except that it is not a sequence database. The specification examples are drawn to the method of identifying a polypeptide wherein the first step of the method is to generate/create a reference polypeptide database for a specific "class" species and then using this database to identifying a polypeptide in a sample (Example I and II of pg. 66-78). The specification does not teach the method of the method of identifying a polypeptide using ***any*** reference polypeptide database that is not a sequence database (e.g. both commercial and known peptide databases such as MASCOT and MOWSE, which are peptide databases for molecular weights of peptides) for identification of the polypeptide in the sample.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.).

With the exception of the method of identifying a polypeptide wherein the first step of the method is to generate/create a reference polypeptide database for a specific "class" species and then using this database to identifying a polypeptide in a sample disclosed by the specification, the skilled artisan cannot envision the method of identifying a polypeptide using ***any*** reference polypeptide database that is not a sequence database for identification of the polypeptide in the sample. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying a polypeptide by using a reference database. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In *re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented

> what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

In the present instance, the claimed method of identifying a polypeptide wherein the determined characteristic of the polypeptide in the sample is compared to the characteristic found in an annotated polypeptide index with the proviso that the annotated polypeptide index is not a sequence database to identify the polypeptide in the sample. The specification does not teach the method of identifying a polypeptide using ***any*** reference polypeptide database that is not a sequence database (e.g. both commercial and known peptide databases such as MASCOT and MOWSE, which are peptide databases for molecular weights of peptides) for identification of the polypeptide in the sample. Therefore, only the method of identifying a polypeptide wherein the first step of the method is to generate/create a reference polypeptide database for a specific "class" species and then using this database to identifying a polypeptide in a sample, but not the full breadth of the claim method meet the written description provision of 35 U.S.C 112, first paragraph.

16. Claims 11-23, and 44-52 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. (This is a new matter rejection.)

The instant claimed methods briefly recite the method of identifying a polypeptide wherein the determined characteristic of the polypeptide in the sample is compared to the

characteristic found in an annotated polypeptide index with the proviso that the annotated polypeptide index is not a sequence database to identify the polypeptide in the sample.

The recitation of 'with the proviso that the annotated polypeptide index is not a sequence database' claimed in claims 1 and 13, have no clear support in the specification and the claims as originally filed. The specification in page 18 disclosed '*A polypeptide identification index can be based on deduced characteristics associated with a polypeptide, for example, characteristics predicted based on sequence information such as genomic sequence, cDNA sequence, or EST database*' (22-26) and on page 26 disclosed '*A polypeptide identification index can be based on deduced characteristics of a polypeptide, for example, one or more characteristics deduced from genetic sequence databases or can be determined empirically*' is not support for '*with the proviso that the annotated polypeptide index is not a sequence database*'. Because the limitation of the specification recites that the annotated polypeptide index would encompassed the sequence database, it does not support the limitation of the claim, which recites the claimed annotated polypeptide index exclude sequence database. Therefore, the scope of the invention as originally disclosed in the specification would not encompass the scope of the limitation of with the proviso that the annotated polypeptide index is not a sequence database.

If applicants disagree, applicant should present a detailed analysis as to why the claimed subject matter has clear support in the specification.

17. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

18. Claims 11-23, and 44-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Clarification is need as to whether the term "second characteristic" is synonymous with the term "empirically determined characteristic".

Claim Rejections - 35 USC § 102

19. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

20. Claims 1, and 4-8 are rejected under 35 U.S.C. 102(a) as being anticipated by Masselon et al. (*Anal. Chem.*, **2000**, 72:1918-1924).

Masselon et al. disclose the method of identifying the polypeptides in a sample mixture by mass spectrometric approach wherein the mass data of the sample is compared with the mass data of a database in order to identify the polypeptides in a sample mixture (pg. 1922, fig. 3 ; pg. 1921, left col., lines 25-29 ; pg. 1921, right col., lines 13-26). The method comprises of obtaining the mass of the peptide fragment by mass spectrometry of the sample (refers to step (a) of claim 1) and then the search for the identification of the polypeptides. The search is performed by first generating a list of the masses of all possible tryptic fragments protein (empirically determined characteristic/second characteristic) and compared to a list of masses of

the parent ions to create a database (annotated polypeptide index) to use for the identification of the polypeptides in a sample (refers to step (b) and (c) of claim 1). The fragment mass is determined by the accuracy of the 1 ppm or greater (pg. 1919, right col., lines 28-33) (refers to claims 4-8). Therefore, the method of Masselon et al. anticipates the presently claimed method.

21. Claims 1-2, 8-12, and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by Yates, III (*J. Mass Spectrom.*, **1998**, 33(1):1-19).

Yates, III disclosed two different types of methods identifying polypeptides by mass spectrometry one is mass mapping (pg. 8, right col., lines 10-13 to pg. 9, left col., lines 1-5) and the second is by 'shotgun' identification of proteins in mixtures (pg. 13, right col., lines 16-33 to pg. 14, left col., lines 1-5; fig. 8). In mass mapping the determined mass is compared with database information of one organism to identify the similar or homologous protein of another organism to identify the polypeptide (pg. 8, right col., lines 10-13 to pg. 9, left col., lines 1-5). In the 'shotgun' identification of proteins in mixtures, the proteins in the mixture is digested and then the protein fragment of the digested mixture is analyzed by mass spectrometry (pg. 13, right col., lines 16-21). The data is compared using computer algorithms and databases in order to reconstruct the identities of the proteins (pg. 13, right col., lines 31-33 to pg. 14, left col., lines 1-5). Therefore, the methods of Yates, III anticipate the presently claimed method.

22. Claims 1-2, 12, 44, and 50 are rejected under 35 U.S.C. 102(b) as being anticipated by Clauser et al. (*Proc. Natl. Acad. Sci.*, **1995**, 92:5072-5076).

Clauser et al. disclosed a method of identifying and characterizing protein by mass spectrometry (pg. 5073, left col., lines 41-63; fig. 2). The method step comprise excised protein spot from several gels, pooling spots of identical mass pI (second characteristic), and peptide separation by HPLC (chromatography) (pg. 5073, left col., lines 46-49; fig. 2) (refers to claim 12, 44, and 50); determining the mass of each of these peptides by mass spectrometry (first characteristic) (pg. 5073, left col., lines 54-55; fig. 2); and search peptide mass database (annotated polypeptide index) with the experimentally determine "characteristics" to identify the protein (pg. 5073, left col., lines 60-63; fig. 2). The peptide database is MOWSE, which is a non-sequence database (pg. 5073; left col., lines 34-37). Therefore, the method of Clauser et al. anticipates the presently claimed method.

Claim Rejections - 35 USC § 103

23. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

24. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

25. Claims 1-12, and 44-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clauser et al. (*Proc. Natl. Acad. Sci.*, **1995**, 92:5072-5076) and Gygi et al. (*Nat. Biotechnol.*; 17(10):994-999; 1999).

Clauser et al. disclosed a method of identifying and characterizing protein by mass spectrometry (pg. 5073, left col., lines 41-63; fig. 2). The method step comprise excised protein spot from several gels pooling spots of identical mass pI (second characteristic), and peptide separation by HPLC (chromatography) (pg. 5073, left col., lines 46-49; fig. 2) (refers to claim 12, 44, and 50); determining the mass of each of these peptides by mass spectrometry (first characteristic) (pg. 5073, left col., lines 54-55; fig. 2); and search peptide mass database (annotated polypeptide index) with the experimentally determine "characteristics" to identify the protein (pg. 5073, left col., lines 60-63; fig. 2). The peptide database is MOWSE, which is a non-sequence database (pg. 5073; left col., lines 34-37).

Additionally, the limitation of the number of characteristics of the polypeptide (e.g. claims 2, and 9-11), the type of chromatography (e.g. claims 45-49, and the limitation of the degree of mass accuracy (e.g. claims 4-8) would be considered a choice as experimental design and is considered within the purview of the prior art.

The method of Clauser et al. does not expressly disclose method step of quantitating the amount of polypeptide in a sample.

Gygi et al. disclose a method of quantitative analysis of protein using isotope-coded affinity tags (Abstract; pg. 994, right col., lines 6-9; pg. 996, left col., line 10 to right col., line 10; fig. 2 and 3).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include the method step of quantitating the amount of polypeptide in a sample as taught by Gygi et al. in the method of Clauser et al. One of ordinary skill in the art would have been motivated to include the method step of quantitating the amount of polypeptide in a sample in the method of Clauser et al. for the advantage of the relative quantities as well as the identity of the polypeptide in a single automated operation (Gygi: pg 995, right column, line 1-2) since both Clauser et al. and Gygi et al. disclose the method of detecting polypeptide by mass spectrometry (Clauser: pg. 5073, left col., lines 54-55; Gygi: pg. 995, left col., line 7 to right col., line 2). One of ordinary skill in the art would have reasonably expectation of success in the combination of Clauser et al. and Gygi et al. because Gygi et al. disclose examples in the application of the method to quantitative analysis of protein in different sample type such as standard mixture and proteome analysis (pg. 996-998).

26. Claims 13-23 and 51-52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Clauser et al. (*Proc. Natl. Acad. Sci.*, **1995**, 92:5072-5076) and Gygi et al. (*Nat. Biotechnol.*; 17(10):994-999; 1999).

Clauser et al. disclosed a method of identifying and characterizing protein by mass spectrometry (pg. 5073, left col., lines 41-63; fig. 2). The method step comprise excised protein spot from several gels pooling spots of identical mass pI (second characteristic), and peptide

separation by HPLC (chromatography) (pg. 5073, left col., lines 46-49; fig. 2) (refers to claim 14, and 23); determining the mass of each of these peptides by mass spectrometry (first characteristic) (pg. 5073, left col., lines 54-55; fig. 2); and search peptide mass database (annotated polypeptide index) with the experimentally determine "characteristics" to identify the protein (pg. 5073, left col., lines 60-63; fig. 2). The peptide database is MOWSE, which is a non-sequence database (pg. 5073; left col., lines 34-37).

Additionally, the limitation of the number of characteristics of the polypeptide (e.g. claims 14, and 20-22), and the limitation of the degree of mass accuracy (e.g. claims 15-19) would be considered a choice as experimental design and is considered within the purview of the prior art.

The method of Clauser et al. does not expressly disclose method step of quantitating the amount of polypeptide in a sample.

Gygi et al. disclose a method of quantitative analysis of protein using isotope-coded affinity tags (Abstract; pg. 994, right col., lines 6-9; pg. 996, left col., line 10 to right col., line 10; fig. 2 and 3).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to include the method step of quantitating the amount of polypeptide in a sample as taught by Gygi et al. in the method of Clauser et al. One of ordinary skill in the art would have been motivated to include the method step of quantitating the amount of polypeptide in a sample in the method of Clauser et al. for the advantage of the relative quantities as well as the identity of the polypeptide in a single automated operation (Gygi: pg 995, right column, line 1-2) since both Clauser et al. and Gygi et al. disclose the method of detecting polypeptide by

mass spectrometry (Clauser: pg. 5073, left col., lines 54-55; Gygi: pg. 995, left col., line 7 to right col., line 2). One of ordinary skill in the art would have reasonably expectation of success in the combination of Clauser et al. and Gygi et al. because Gygi et al. disclose examples in the application of the method to quantitative analysis of protein in different sample type such as standard mixture and proteome analysis (pg. 996-998).

Response to Arguments

27. Applicant's arguments with respect to claims 1-23, and 44-52 have been considered but are moot in view of the new ground(s) of rejection.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to My-Chau T. Tran whose telephone number is 703-305-6999. The examiner can normally be reached on Monday: 8:00-2:30; Tuesday-Thursday: 7:30-5:00; Friday: 8:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew J. Wang can be reached on 703-306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

mct
December 16, 2003

PADMASHRI PONNALURI
PRIMARY EXAMINER